

In the Specification:

A Substitute Specification (including amendments to the claims) and a marked-up copy of the as-filed Specification and Abstract is provided herewith.

In the Claims:

Please cancel claims ~~1, 25, 37 and 82~~ and enter new claims 84-134 therefor:

~~84.~~ (New) A chimeric peptide-nucleic acid construct comprising:

- (a) a mitochondria-specific signal peptide, wherein the peptide does not comprise a KDEL signal sequence,
- (b) a linkage agent covalently linked to an amino acid at the carboxy-terminal end of the signal peptide, and
- (c) a linear nucleic acid, wherein said nucleic acid is covalently linked to the linkage agent,

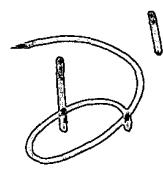
whereby the signal peptide is linked to the nucleic acid via the linkage agent in the construct so that the chimeric peptide-nucleic acid construct enters mitochondria.

~~85.~~ (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the nucleic acid has secondary structure.

86. (New) The chimeric peptide-nucleic acid construct of claim 85, wherein the nucleic acid comprises a partially palindromic sequence.

87. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the nucleic acid is ribonucleic acid or deoxyribonucleic acid, and wherein said peptide has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:22.

88. (New) The chimeric peptide-nucleic acid construct according to claim 84, wherein phosphodiester bonds of the nucleic acid are substituted with phosphorus thioate bonds.



89. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the nucleic acid comprises a reactive linkage group.
90. (New) The chimeric peptide-nucleic acid construct of claim 89, wherein the reactive linkage group contains an amino function and the linkage agent contains an amino-reactive group.
91. (New) The chimeric peptide-nucleic acid construct of claim 89, wherein the reactive linkage group contains a thiol function and the linkage agent contains a thiol-reactive group.
92. (New) The chimeric peptide-nucleic acid construct of claim 89, wherein the linkage group is bound to the nucleic acid via a spacer comprising at least two carbon atoms.
93. (New) The chimeric peptide-nucleic acid construct of claim 92 wherein the linkage group present is bound to the nucleic acid via a spacer comprising six carbon atoms.
94. (New) The chimeric peptide-nucleic acid construct of claim 90, wherein the linkage group is localized at the 3' hydroxy/phosphate terminus or at the 5' hydroxy/phosphate terminus of the linear nucleic acid.
95. (New) The chimerical peptide-nucleic acid construct of claim 94, wherein an additional nucleic acid, an antisense oligonucleotide, a messenger RNAs or a transcribable and/or replicative gene is covalently linked with the 5' terminus and/or 3' terminus of the nucleic acid.
96. (New) The chimeric peptide-nucleic acid construct of claim 95, wherein the promoter is a mitochondrial promoter.

97. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the signal peptide has a reactive amino acid at the carboxy-terminal end and wherein the linkage agent contains an amino-reactive or thiol-reactive group.

98. (New) The chimeric peptide-nucleic acid construct of claim 97, wherein the reactive amino acid at the carboxyl-terminal end is lysine or cysteine.

99. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the signal peptide comprises a mitochondria-specific peptidase cleavage site.

100. (New) The chimeric peptide-nucleic acid construct of claim 99, wherein the peptide consists of the mitochondria-specific cleavable signal peptide of human mitochondrial ornithine transcarbamylase, extended by an cysteine at the C terminus.

101. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent is a bifunctional or a heterobifunctional cross-linker.

102. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent contains thiol-reactive and/or amino-reactive groupings when the signal peptide and the nucleic acid carry thiol and/or amino groups as linkage sites.

103. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent is m-maleimido-benzoyl-N-hydroxy-succinimide ester or a derivative thereof.

104. (New) The chimeric peptide-nucleic acid construct of claim 84, wherein the molecule penetrates mitochondrial membranes by utilizing natural transport mechanisms.

105. (New) A chimeric peptide-nucleic acid construct of a linear-cyclic nucleic acid molecule, wherein the molecule comprises at least one replication origin and wherein both ends of the

molecule are cyclized, said cyclized plasmid having at least one cyclic end having a modified nucleotide which via a linkage agent is linked with a mitochondria-specific or membrane-specific signal peptide.

106. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the nucleic acid portion further comprises at least one promoter.
107. (New) The chimeric peptide-nucleic acid construct of claim 106, wherein at least one promoter is a mitochondrial promoter.
108. (New) The chimeric peptide-nucleic acid construct of claim 107, wherein the mitochondrial promoter is the mitochondrial promoter of the light strand.
109. (New) The chimeric peptide-nucleic acid construct of claim 106, wherein the molecule comprises further mitochondrial transcription-regulatory sequences.
110. (New) The chimeric peptide-nucleic acid construct of claim 109, wherein the transcription-regulatory sequences are 3' of the promoter.
111. (New) The chimeric peptide-nucleic acid construct of claim 109, wherein the transcription-regulatory sequences comprise elements of the mitochondrial H-strand and L-strand transcription control elements.
112. (New) The chimeric peptide-nucleic acid construct of claim 111, wherein said L-strand transcription control elements are conserved-sequence-blocks.
113. (New) The chimeric peptide-nucleic acid construct of claim 108, wherein the transcription-regulatory sequences comprise a binding sequence of a mitochondrial transcription termination factor.

114. (New) The chimeric peptide-nucleic acid construct of claim 113, wherein the transcription termination factor is a bidirectionally acting transcription termination factor.

115. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the replication origin is a mitochondrial replication origin.

116. (New) The chimeric peptide-nucleic acid construct of claim 115, wherein the replication origin is the replication origin of the heavy mtDNA strand and comprises at least one 'conserved sequence block'.

117. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the plasmid nucleic acid portion further comprises a selection gene.

118. (New) The chimeric peptide-nucleic acid construct of claim 117, wherein the selection gene is an antibiotic-resistance gene.

119. (New) The chimeric peptide-nucleic acid construct of claim 118, wherein the antibiotic-resistance gene is an oligomycin-resistance gene or a chloramphenicol-resistance gene.

120. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the molecule further comprises a multiple cloning site.

121. (New) The chimeric peptide-nucleic acid construct of claim 120, wherein the multiple cloning site comprises recognition sequences for restriction endonucleases which do not occur in another site of the plasmid.

122. (New) The chimeric peptide-nucleic acid construct of claim 121, wherein the multiple cloning site is arranged in the 3' direction of the promoter and in the 5' direction of the transcription termination site.

123. (New) The chimeric peptide-nucleic acid construct of claim 121, wherein the multiple cloning site is arranged in the 5' direction of the selection gene.

124. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the ends of the nucleic acid are covalently joined to the peptide.

125. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the linear-cyclic plasmid nucleic acid portion has 5' overhangs which do not have a palindromic sequence and which sequences are not complementary to one another.

126. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein the ends of the nucleic acid construct are cyclized via synthetic oligonucleotides.

127. (New) The chimeric peptide-nucleic acid construct of claim 105, wherein a restriction endonuclease is to generate overhanging ends in the linear-cyclic plasmid nucleic acid portion of the construct.

128. (New) The chimeric peptide-nucleic acid construct of claim 127, wherein the restriction endonuclease is *BsaI*.

~~129.~~ (New) A method for the production of a chimeric peptide-nucleic acid construct which enters mitochondria, said method comprising the steps of:

(a) reacting a nucleic acid or oligonucleotide containing a functional linkage group having a linkage agent to form a construct,

(b) reacting of the construct of (a) with amino acids at the carboxy-terminal end of a peptide containing a signal sequence, wherein the signal sequence is not a KDEL signal sequence, to form a chimeric peptide-nucleic acid linked construct; and